Complete Summary

GUIDELINE TITLE

Heart Failure Society of America guidelines for management of patients with heart failure caused by left ventricular systolic dysfunction: pharmacological approaches.

BIBLIOGRAPHIC SOURCE(S)

Heart Failure Society of America. Heart Failure Society of America (HFSA) practice guidelines. HFSA guidelines for management of patients with heart failure caused by left ventricular systolic dysfunction--pharmacological approaches. J Card Fail 1999 Dec;5(4):357-82. [130 references]

HFSA guidelines for management of patients with heart failure caused by left ventricular systolic dysfunction--pharmacological approaches. Heart Failure Society of America. Pharmacotherapy 2000 May;20(5):495-522. [130 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Heart failure caused by left ventricular systolic dysfunction

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice

Internal Medicine
Nursing
Pharmacology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based clinical practice guidelines on the pharmacological management of patients with heart failure caused by left ventricular systolic dysfunction

TARGET POPULATION

Patients with heart failure caused by left ventricular systolic dysfunction

INTERVENTIONS AND PRACTICES CONSIDERED

1. Pharmacologic Management
    - Beta-adrenergic receptor blockers (metoprolol controlled release/extended release [CR/XL], bisoprolol, carvedilol. bucindolol)
    - Digoxin
    - Anticoagulants (warfarin)
    - Antiplatelets (aspirin or alternatives, ticlopidine, clopidogrel)
    - Angiotensin-converting enzyme inhibitors
    - Hydralazine in combination with isosorbide dinitrate
    - Antiarrhythmic agents (amiodarone)
    - Aldosterone antagonists (spironolactone)
    - Diuretics (loop, thiazides)

    Note: Angiotensin II receptor blockers (losartan, candesartan, valsartan) are considered for patients with documented intolerance to angiotensin-converting enzyme inhibitors. Immunosuppressive therapies (prednisone, cyclosporine, high-dose immune globulin) are considered for patients with myocarditis but not recommended.

2. Implantable Cardiac Defibrillator (ICD) Placement

MAJOR OUTCOMES CONSIDERED

- Rates or risk of death (all cause or cardiovascular related)
- Rates or risk of hospitalization, including hospitalization for worsening heart failure
- Rates or risk of arrhythmia

- Need for co-medications
- Quality of life
- Improvement in left ventricular ejection fraction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Strength of Evidence

A. Well-designed and adequately controlled clinical trials performed in relevant patient populations.
B. Other useful investigations, including cohort studies.
C. Expert opinion.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

During the development of the guidelines, the guideline committee had several face-to-face meetings; however, a substantial portion of the work was accomplished through the assiduous use of teleconferencing. A draft representing the committee's consensus opinion was completed in May 1999 and submitted to the Executive Council for approval. The members of the Executive Council had the opportunity to provide written comments, and areas of concern were adjudicated by teleconference between the committee and members of the Executive Council.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The Executive Council met to discuss the guidelines in September 1999, at which time the major recommendations were unanimously approved. Subsequently, the major recommendations were presented to the membership of the Society during the Annual Scientific Meeting. The society membership provided important insights, many of which were then incorporated into the final document. Finally, after submission of final comments, the complete text of the guidelines document was approved by the Executive Council and the Guideline Committee during a telephone conference held in October, 1999. Thus, the guidelines underwent a scrupulous review process with both comments and consensus being obtained from a large group of stakeholders.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC):

The grading scheme (strength of evidence) and the criteria for New York Heart Association functional classification for chronic heart failure patients' functional capacity is defined at the end of the Major Recommendations field.

<u>Recommendations for Pharmacological Therapy: Left Ventricular Systolic Dysfunction</u>

Beta-Adrenergic Receptor Blockers

1. Beta-blocker therapy should be routinely administered to clinically stable patients with left ventricular systolic dysfunction (left ventricular ejection fraction less than or equal to 40%) and mild to moderate heart failure symptoms (that is, New York Heart Association class II-III) who are on standard therapy, which typically includes angiotensin-converting enzyme (ACE) inhibitors, diuretics as needed to control fluid retention, and digoxin (Strength of Evidence = A).
2. Beta-blocker therapy should be considered for patients with left ventricular systolic dysfunction (left ventricular ejection fraction less than or equal to 40%) who are asymptomatic (that is, New York Heart Association class I) and on standard therapy, including angiotensin-converting enzyme inhibitors (Strength of Evidence = C).
3. To maximize patient safety, a period of clinical stability on standard therapy should occur before beta-blocker therapy is instituted. Initiation of beta-blocker therapy in patients with heart failure requires a careful baseline evaluation of clinical status (Strength of Evidence = B).
4. There is insufficient evidence to recommend the use of beta-blocker therapy for inpatients or outpatients with symptoms of heart failure at rest (that is, New York Heart Association class IV) (Strength of Evidence = C).
5. Beta-blocker therapy should be initiated at low doses and up-titrated slowly, generally no sooner than at 2-week intervals. Clinical re-evaluation should occur at each titration point and with worsening of patient symptoms. Patients who develop worsening heart failure or other side effects after drug initiation or during titration require adjustment of concomitant medications. These patients may also require a reduction in beta-blocker dose and, in some cases, temporary or permanent withdrawal of this therapy (Strength of Evidence = B).
6. In general, patients who experience a deterioration in clinical status or symptomatic exacerbation of heart failure during chronic maintenance treatment should be continued on beta-blocker therapy (Strength of Evidence = C).
7. Patient education regarding early recognition of symptom exacerbation and side effects is considered important. If clinical uncertainty exists, consultation with clinicians who have expertise in heart failure and/or specialized programs with experience in beta-blocker use in patients with heart failure is recommended (Strength of Evidence = B).

Digoxin

1. Digoxin should be considered for patients who have symptoms of heart failure (New York Heart Association class II-III, Strength of Evidence = A and New York Heart Association class IV, Strength of Evidence = C) caused by left ventricular systolic dysfunction while receiving standard therapy.
2. In the majority of patients, the dosage of digoxin should be 0.125 milligrams to 0.25 milligrams daily (Strength of Evidence = C).
3. In patients with heart failure and atrial fibrillation with a rapid ventricular response, the administration of high doses of digoxin (greater than 0.25 milligrams) for the purpose of rate control is not recommended. When necessary, additional rate control should be achieved by the addition of beta-blocker therapy or amiodarone (Strength of Evidence = C).

Anticoagulation

1. All patients with heart failure and atrial fibrillation should be treated with warfarin (goal, international normalized ratio [INR] 2.0 to 3.0) unless contraindicated (Strength of Evidence = A).
2. Warfarin anticoagulation merits consideration for patients with left ventricular ejection fraction of 35% or less. Careful assessment of the risks and benefits of anticoagulation should be undertaken in individual patients (Strength of Evidence = B).

Antiplatelet Drugs

1. With regard to the concomitant use of angiotensin-converting enzyme inhibitors and acetylsalicylic acid, each medication should be considered on its own merit for individual patients. Currently, there is insufficient evidence concerning the potential negative therapeutic interaction between acetylsalicylic acid and angiotensin-converting enzyme inhibitors to warrant withholding either of these medications in which an indication exists (Strength of Evidence = C).

Angiotensin II Receptor Blockers

1. Angiotensin-converting enzyme inhibitors rather than angiotensin II receptor blockers continue to be the agents of choice for blockade of the renin-angiotensin system in heart failure, and they remain the cornerstone of standard therapy for patients with left ventricular systolic dysfunction with or without symptomatic heart failure (Strength of Evidence = A).
2. All efforts should be made to achieve angiotensin-converting enzyme inhibitor use in patients with heart failure caused by left ventricular dysfunction. Patients who are truly intolerant to angiotensin-converting enzyme inhibitors should be considered for treatment with the combination of hydralazine and isosorbide dinitrate (Strength of Evidence = B) or an angiotensin II receptor blocker (Strength of Evidence = C).

Antiarrhythmic Drug and Device Therapy

1. Based on the inconclusive results of clinical trials with amiodarone and its known toxicity, this drug is not recommended for the primary prevention of death in patients with chronic heart failure (Strength of Evidence = A).
2. Based on evidence from a number of clinical trials that included patients with heart failure and reduced ejection fractions, it is recommended that patients with heart failure who have been resuscitated from primary ventricular fibrillation or who have experienced hemodynamically destabilizing sustained ventricular tachycardia be treated with implantable cardiac defibrillators (Strength of Evidence = B).
3. Amiodarone is the preferred drug when antiarrhythmic therapy in indicated in patients with heart failure for supraventricular tachycardia not controlled by digoxin or beta-blocker or for patients with life-threatening ventricular arrhythmia who are not candidates for implantable cardiac defibrillator placement (Strength of Evidence = B).

Aldosterone Antagonists

1. Administration of the aldosterone antagonist spironolactone at low dose (that is, 12.5 milligrams to 25 milligrams once daily) should be considered for patients receiving standard therapy who have severe heart failure (with recent or current New York Heart Association class IV) caused by left ventricular systolic dysfunction. Patients treated in this manner should have a normal serum potassium level (less than 5.0 millimoles per liter) and adequate renal function (creatinine less than 2.5 milligrams per deciliter) (Strength of Evidence = A). Serum potassium concentration should be monitored after the first week and at regular intervals thereafter and after any change in dose of spironolactone or in the dose of concomitant medications that may affect potassium balance. Consideration should be given to lowering or eliminating supplemental potassium (Strength of Evidence = A).

Myocarditis: Current Treatment

1. An evidence-based approach to treatment suggests than an effective therapy for myocarditis remains to be identified. Routine use of immunosuppressive therapies cannot be recommended for patients with myocarditis (Strength of Evidence = B).

Strength of Evidence:

- Strength of Evidence A: Well-designed and adequately controlled clinical trials performed in relevant patient populations.
- Strength of Evidence B: Other useful investigations, including cohort studies.
- Strength of Evidence C: Expert opinion.

Criteria for New York Heart Association Functional Classification for Chronic Heart Failure Patients' Functional Capacity

- Class 1: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea.
- Class 2: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
- Class 3: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.
- Class 4: Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increase.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients with heart failure caused by left ventricular systolic dysfunction may decrease mortality rates, hospitalization rates, and need for co-interventions, thus improving length and quality of life for patients. The substantial beneficial effect of beta-blocker therapy on mortality and hospitalizations has been well shown in clinical trials of symptomatic patients (New York Heart Association Functional Classification class II-III) treated with carvedilol, bisoprolol, or metoprolol controlled release/extended release.

Data from one Prevention Trial prospectively illustrated the efficacy of angiotensin-converting enzyme inhibitors in delaying the onset of heart failure symptoms and the need for treatment or hospitalization for heart failure in asymptomatic patients with a left ventricular ejection fractions less than or equal to 35 percent.

A large body of evidence supports the efficacy of digoxin in patients with symptomatic heart failure caused by left ventricular systolic dysfunction. Digoxin has been shown to decrease hospitalizations, as well as emergency room visits; decrease the need for co-intervention; and improve exercise capacity. Taken as a whole, these clinical trial data provide support for digoxin's beneficial effect on morbidity and neutral effect on mortality. In a clinical trial to determine the effect of a low dose of spironolactone on survival in severely symptomatic (with recent or current New York Heart Association class IV) heart failure patients treated with angiotensin-converting enzyme inhibitor, loop diuretic, and, in many case, digoxin, the results showed a reduction in the risk of death from progressive heart failure or sudden death in patients treated with spironolactone.

POTENTIAL HARMS

- Initiation of beta-blocker therapy has the potential to worsen heart failure signs and symptoms. Worsening heart failure is typically reflected by increasing fatigue, lower exercise tolerance, and weight gain. Increased diuretic doses may be required for signs of fluid retention. Beta-blockers can also produce vasodilatory side effects (e.g., hypotension).
- There is a risk of digoxin toxicity with increasing doses of the drug.
- There is known toxicity with amiodarone.
- Side effects of angiotensin-converting enzyme inhibitors include cough, renal dysfunction, hyperkalemia, and persistent symptomatic hypotension.
- Spironolactone can cause hyperkalemia; in addition; gynecomastia or breast pain was reported in 10% of men randomized to spironolactone (versus 1% in the placebo group) in one clinical trial.

Subgroups Most Likely to Be Harmed:

The risk for worsening heart failure signs and symptoms with initiation of beta-blocker therapy increases with the underlying severity of the heart failure that is present.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Recommendations are presented as applicable without regard to race or gender. However, the guideline developers acknowledge that currently available clinical trial data do not provide completely adequate information in this regard.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Dec

GUIDELINE DEVELOPER(S)

Heart Failure Society of America, Inc - Disease Specific Society

SOURCE(S) OF FUNDING

Heart Failure Society of America (HFSA)

GUIDELINE COMMITTEE

Guideline Committee for the Heart Failure Society of America; Executive Council for the Heart Failure Society of America

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, a comprehensive guideline for heart failure will be available January 2003.

GUIDELINE AVAILABILITY

Electronic copies: Available (in Portable Document Format) from the Heart Failure Society of America (HFSA) Web site.

Print copies: Available from the Heart Failure Society of America, Inc. (HFSA), Court International - Suite 238N, 2550 University Avenue West, Saint Paul, MN 55114; e-mail, info@hfsa.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 16, 2001. The information was verified by the guideline developer as of October 12, 2001.

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